REMARKS

I. Status Summary

Claims 1, 2, 4, 18, 19, 21-24, and 25 are pending in the subject application. Claims 18, 19, 22, and 23 were previously withdrawn. Claims 1, 2, 4, 21, 24, and 25 have currently been examined and are pending in the Patent Office.

The Patent Office maintains that the instant claims do not have priority to the filing date of the Priority Document (Australian Patent Application No. 2003/901425), and the effective filing date of the instant claims is the filing date of the instant application, or March 23, 2004.

Claims 4 and 21 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention.

The Patent Office has rejected claims 4 and 21 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

Claims 1, 2, 4, 21, 24, and 25 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Patent Office has rejected claims 1, 2, 24, and 25 under 35 U.S.C. §103(a) as allegedly being unpatentable over Claes *et al.* (2001) *Am J of Human Genet* **68**:1327-1332 (hereinafter referred to as "Claes *et al.*").

Claim 1 has been amended herein. Support for the amendments to claim 1 can be found throughout the specification as filed, including particularly at page 5, lines 2-24; page 14, lines 11-16; and page 14, lines 29-32. Further support can be found in Figure 1 and in original claims 1 and 20. No new matter has been added.

New claim 26 has been added. Support for new claim 26 can be found throughout the specification as filed, including particularly at page 5, lines 2-24; page 14, lines 11-16; and page 14, lines 29-32. Further support can be found in Figure 1 and in original claims 1 and 20. No new matter has been added.

New claim 27 has been added. Support for new claim 27 can be found throughout the specification as filed, including particularly at page 40, line 22, through page 41, line 17. No new matter has been added.

Claims 2, 4, 18, 19, and 21-25 have been canceled without prejudice. As such, claims 1, 26, and 27 are currently pending in the instant application.

Reconsideration of the application based on the arguments set forth herein is respectfully requested.

II. Response to the Objection to the Priority Claim

The Patent Office maintains that the claims are not properly supported by the Priority Document because the element of testing for an alteration in a regulatory region is not disclosed in the Priority Document.

Without acquiescing to the contentions of the Patent Office, applicants respectfully submit that claims 2, 4, 21, 24, and 25 have been canceled herein. As such, the instant objection is believed to be rendered moot with respect to these claims.

Regarding claim 1, applicants respectfully maintain that the Priority Document teaches the SCN1A gene is the most frequently mutated gene associated with SMEI. As such, the Priority Document discloses methods for testing a patient for SCN1A gene mutations in evaluating patients for SMEI. See, for example, page 5, lines 8-13 of the Priority Document. Applicants respectfully submit that "gene", as used in the context of the Priority Document disclosure, is believed to include both regulatory and non-regulatory regions. Therefore, applicants respectfully maintain that claim 1 is believed to be adequately supported by the Priority Document.

Although applicants disagree that the element of testing for an alteration in a regulatory region is not supported by the Priority Document, applicants respectfully submit that new claim 26 does not recite this element and is therefore believed to be adequately supported by the Priority Document. Support for new claim 26 can be found throughout the present specification as originally filed and particularly at page 5, lines 2-24; page 14, lines 11-16; and page 14, lines 29-32. Further support can be found in Figure 1 and in original claims 1 and 20. No new matter has been added.

Summarily, applicants respectfully submit that claims 1 and 26 are believed to be adequately supported by the Priority Document. As such, applicants respectfully submit that the priority claim to Australian Patent Application No. 2003/901425 under 35 U.S.C. §119(a)-(d) with respect to claims 1 and 26 is believed to be proper. Thus, applicants respectfully request that the instant objection to the priority claim regarding claims 1 and 26 be withdrawn at this time.

III. Response to the 35 U.S.C. §112, Second Paragraph, Rejection of Claims 4 and 21

Claims 4 and 21 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention.

Without acquiescing to the contentions of the Patent Office applicants respectfully submit that claims 4 and 21 have been canceled without prejudice, therefore mooting the instant rejections with respect to these claims.

Thus, applicants respectfully request that the rejection of claims 4 and 21 under 35 U.S.C. §112, second paragraph, be withdrawn at this time.

IV. Response to the 35 U.S.C. §112, First Paragraph, Written Description Rejection of Claims 4 and 21

The Patent Office has rejected claims 4 and 21 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

Without acquiescing to the contentions of the Patent Office applicants respectfully submit that claims 4 and 21 have been canceled without prejudice, therefore mooting the instant rejections with respect to these claims.

Thus, applicants respectfully request that the rejection of claims 4 and 21 under 35 U.S.C. §112, first paragraph, be withdrawn at this time.

V. Response to the 35 U.S.C. §112, First Paragraph, Enablement Rejection of Claims 1, 2, 4, 21, 24, and 25

Claims 1, 2, 4, 21, 24, and 25 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

After careful consideration of the rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

Preliminarily, without acquiescing to the contention of the Patent Office, applicants respectfully submit that claims 2, 4, 21, 24, and 25 have been canceled herein. Therefore the instant rejections with respect to these claims are believed to be mooted.

Applicants respectfully submit that claim 1 has been amended herein. In particular, applicants respectfully submit that claim 1 has been amended as follows:

1. A method for determining the likelihood that a human patient suspected of SMEI does or does not have SMEI comprising:

   (1) screening a patient sample for the existence of ~~an alteration~~ a mutation in the SCN1A gene of the patient, including in a regulatory region of the gene, by sequencing the SCN1A gene;

   (2) (a) terminating the process if no ~~alteration~~ mutation is found~~, thereby establishing that the patient likely does not have SMEI~~; or

   (b) identifying the ~~alteration~~ mutation; and

   (3) ascertaining whether the ~~alteration~~ mutation, when one is detected, has previously been detected in a patient clinically diagnosed with SMEI and is therefore considered SMEI associated or has previously been detected in a patient ~~not diagnosed with~~ unaffected by SMEI and is therefore considered non-SMEI associated, or [[is]] if not considered to be either, (i) considering genetic data for the parents of the patient and

establishing whether the mutation has arisen *de novo* or is inherited; and (ii) establishing whether the mutation is a truncating mutation; wherein

(a) the patient is categorized as having a very high probability of having SMEI when the ~~alteration~~ mutation is SMEI associated;

(b) the patient is categorized as having a low probability of having SMEI when the ~~alteration~~ mutation is non-SMEI associated; or

(c) the patient is categorized as having a low probability of SMEI in the case of an inherited mutation, a high probability of SMEI in the case of a *de novo* mutation, and a very high probability of SMEI in the case of a *de novo* mutation which is truncating ~~further analysis is undertaken to establish the likelihood the patient suspected of SMEI does or does not have SMEI when the detected alteration is not considered to be either SMEI associated or non-SMEI associated,~~

~~wherein the detection of a SMEI associated alteration establishes that a patient suspected of SMEI likely does have SMEI.~~

Support for the amendments to claim 1 can be found throughout the specification as filed, including particularly at page 5, lines 2-24; page 14, lines 11-16; and page 14, lines 29-32. Further support can be found in Figure 1 and in original claims 1 and 20. No new matter has been added.

Initially, the Patent Office contends that the specification does not enable methods requiring establishing that a patient likely does not have SMEI when no alteration in the SCN1A gene is found, as recited in step (2)(a) of claim 1. In particular, the Patent Office contends that it is highly unpredictable as to whether or not one would be able to reliably deduce that a patient likely does not have SMEI merely by finding a lack of SCN1A alterations in the SCN1A gene of the patient. In response, without

acquiescing to the contentions of the Patent Office applicants respectfully submit that present claim 1 does not recite "establishing that the patient likely does not have SMEI". As such, applicants respectfully submit that this aspect of the instant rejection is believed to be rendered moot.

Next, the Patent Office contends that methods requiring determining that an alteration is non-SMEI associated if it has been previously detected in a patient not diagnosed with SMEI are not enabled. In response, applicants respectfully submit that claim 1 has been amended to recite, *inter alia*, "ascertaining whether the mutation, when one is detected...has previously been detected in a patient unaffected by SMEI and is therefore considered non-SMEI associated..." As would be appreciated by one of ordinary skill in the art upon review of the instant specification, if the mutation has previously been identified in a patient with no symptoms of SMEI and is not suspected of being affected by SMEI, the mutation will be considered to have no known association with SMEI, i.e. it will be considered non-SMEI associated. This is not to say that the mutation could never be associated with SMEI or that the patient definitively does not have SMEI. Rather, identifying a mutation as non-SMEI associated serves to categorize the patient regarding the probability of having SMEI based upon prior identified mutations associated with SMEI. Indeed, step (3)(b) recites "the patient is categorized as having a low probability of having SMEI when the mutation is non-SMEI associated" (emphasis added). Therefore, applicants respectfully submit that the Patent Office appears to inappropriately require a categorical diagnosis on each occasion when the presently claimed method is designed as an aid for diagnosis and not a definitive test. Indeed, the specification is believed to adequately enable one of ordinary skill in the art to perform the claimed methods and to use the claimed methods as an aid in diagnosing SMEI.

Finally, the Patent Office contends that the specification fails to enable methods requiring an alteration recited as c251A→G as indicated in Table 3 and required by claims 4 and 21. Without acquiescing to the contentions of the Patent Office applicants respectfully submit that claims 4 and 21 have been cancelled herein. As such, this aspect of the instant rejection is believed to be rendered moot.

Therefore, applicants respectfully submit that the claimed method for the determination of the likelihood of SMEI is disclosed and enabled. Applicants reiterate that the instant claimed methods are not directed to a method of diagnosing SMEI, but rather a method of categorizing patients based upon the likelihood that they have SMEI. To elaborate, a conventional diagnostic test involves an analysis of a piece of DNA to establish whether or not a mutation exists, *i.e.*, if the mutation is present the diagnosis will be positive for the disease state, and if the mutation is absent the diagnosis will be negative for the disease state, depending on the nature of the disease. Generally, the test involves amplification of one single and specific portion of a gene to establish whether or not the mutation is present. In contrast to a conventional diagnostic test, the presently claimed subject matter looks at the totality of the genetic landscape for SCN1A.

Applicants respectfully submit that the presently claimed subject matter provides a method to be employed to make a determination of the likelihood of SMEI in circumstances where screening can identify mutations previously detected in patients with SMEI, mutations previously detected in patients unaffected by SMEI, and mutations that have not previously been associated with either. Clearly, any and all mutations in the SCN1A subunit will fall into one of these three categories. Accordingly, a complete method for the determination of the likelihood of SMEI is disclosed and enabled, irrespective of whether the mutation has previously been detected in patients with SMEI.

Accordingly, applicants respectfully submit that the instant 35 U.S.C. §112, first paragraph, enablement rejection of claim 1 has been addressed. Thus, applicants respectfully request that the instant rejection be withdrawn at this time. Allowance of claim 1 is also respectfully requested.

VI. Response to the 35 U.S.C. §103(a) Rejection of Claims 1, 2, 24, and 25 in view of Claes *et al.*

The Patent Office has rejected claims 1, 2, 24, and 25 under 35 U.S.C. §103(a) as allegedly being unpatentable over Claes *et al.* (2001) *Am J of Human Genet* **68**:1327-1332 (hereinafter referred to as "Claes *et al.*"). Particularly, the Patent Office

asserts that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used the explicit teachings of Claes *et al.* to perform an analysis of a patient suspected of SMEI that meets all of the required limitations of the rejected claims.

After careful consideration of the rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

Preliminarily, without acquiescing to the contentions of the Patent Office, applicants respectfully submit that claims 2, 24, and 25 have been canceled herein. Therefore the instant rejections with respect to these claims are believed to be mooted.

Applicants respectfully submit that claim 1 has been amended as discussed hereinabove. In particular, step (3) of claim 1 now recites, *inter alia*, ascertaining whether the mutation, when one is detected, has previously been detected in a patient clinically diagnosed with SMEI and is therefore considered SMEI associated or has previously been detected in a patient unaffected by SMEI and is therefore considered non-SMEI associated, or if not considered to be either, (i) considering genetic data for the parents of the patient and establishing whether the mutation has arisen *de novo* or is inherited; and (ii) establishing whether the mutation is a truncating mutation; wherein (a) the patient is categorized as having a very high probability of having SMEI when the mutation is SMEI associated; (b) the patient is categorized as having a low probability of having SMEI when the mutation is non-SMEI associated; or (c) the patient is categorized as having a low probability of SMEI in the case of an inherited mutation, a high probability of SMEI in the case of a *de novo* mutation, and a very high probability of SMEI in the case of a *de novo* mutation which is truncating. Support for the amendments to claim 1 can be found throughout the specification as filed, including particularly at page 5, lines 2-24; page 14, lines 11-16; and page 14, lines 29-32. Further support can be found in Figure 1 and in original claims 1 and 20. No new matter has been added.

It is believed that Claes et al. does not teach or suggest the methodology of the present claims. Claes et al. does not teach or suggest ascertaining whether the mutation, when one is detected, has previously been detected in a patient clinically

diagnosed with SMEI and is therefore considered SMEI associated or has previously been detected in a patient unaffected by SMEI and is therefore considered non-SMEI associated (step (3)). Rather, Claes et al. at best reports observations regarding mutations identified in 7 SMEI positive subjects. Because Claes et al. started the study with 7 subjects known to be SMEI positive there was no determination whether the identified mutation is SMEI associated or non-SMEI associated, nor would it have been obvious for one of ordinary skill in the art to do so given the disclosure of Claes et al.

Further, Claes et al. does not teach or suggest that if an identified mutation is considered neither SMEI associated or non-SMEI associated, the next step is considering genetic data for the parents of the patient and establishing whether the mutation has arisen *de novo* or is inherited, and establishing whether the mutation is a truncating mutation (steps (3)(i) and (3)(ii)). Again, because Claes et al. merely reports observations in SMEI positive subjects, there is no teaching or suggestion regarding the analysis of the nature of a mutation post-identification.

Finally, Claes et al. fails to teach the categorization of a patient based upon their probability of having SMEI. In particular, Claes et al. fails to teach or suggest the steps of (3)(a), (3)(b) or (3)(c) of claim 1. As noted above, because the subjects described in Claes et al. were known to have SMEI, it is axiomatic that they would not have been classified based upon their probability of having SMEI.

As such, applicants respectfully submit that Claes et al. fails to teach the subject matter of present claim 1. In merely reporting the observations of 7 subjects known to have SMEI, Claes et al. gives no consideration to the method steps and analysis required to determine the likelihood a patient suspected of having SMEI does or does not have SMEI. Thus, given the vast discrepancy in the disclosure of Claes et al. and present claim 1, applicants respectfully submit that one of ordinary skill in the art would not consider the subject matter of claim 1 to be obvious over Claes et al.

Furthermore, given that Claes et al. fails to teach numerous aspects of present claim 1, applicants respectfully submit that Claes et al. does not constitute enabling prior art that would provide one of ordinary skill in the art a reasonable expectation of success in practicing the claimed method. The observations disclosed in Claes et al. regarding the 7 subjects known to have SMEI do not provide a reasonable expectation

of success to one of ordinary skill in the art to develop and carry out the method set forth in claim 1. In particular, one of ordinary skill in the art would not have a reasonable expectation of success in determining whether an identified mutation is SMEI associated or non-SMEI associated, or if neither, considering genetic data for the parents of the patient and establishing whether the mutation has arisen *de novo* or is inherited, and establishing whether the mutation is a truncating mutation, given the absence of any teaching or suggestion of these aspects in Claes et al. Further, one of ordinary skill in the art would not have a reasonable expectation of success in categorizing or classifying a patient based upon their probability of having SMEI based upon these determinations since Claes et al. makes no mention of such method steps. Taken together, applicants respectfully submit that Claes et al. fails to provide one of ordinary skill in the art a reasonable expectation of success in practicing the claimed method and therefore fails to support a rejection under 35 U.S.C. §103(a).

Hence, applicants respectfully submit that the instant 35 U.S.C. §103(a) rejection of claim 1 as allegedly being unpatentable over Claes *et al.* has been addressed. Accordingly, applicants respectfully request that the rejection of claim 1 be withdrawn at this time. A Notice of Allowance directed to claim 1 is also respectfully requested.

DISCUSSION OF NEW CLAIMS

New claims 26 and 27 have been added. Support for new claims 26 and 27 can be found throughout the specification as filed, including particularly at page 5, lines 2-24; page 14, lines 11-16; page 14, lines 29-32; and page 40, line 22, through page 41, line 17. Further support can be found in Figure 1 and in original claims 1 and 20. No new matter has been added.

Applicants respectfully submit that new claims 26 and 27 are believed to be patentable for at least the reasons discussed hereinabove. As such, applicants respectfully request a Notice of Allowance.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

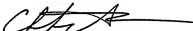
If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any other fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,

JENKINS, WILSON, TAYLOR, & HUNT, P.A.

Date: February 19, 2009 By: 

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